WE CLAIM:

1. A method for making a hypermutable, antibody producing cell, comprising introducing into a cell capable of producing antibodies a polynucleotide comprising a dominant negative allele of a mismatch repair gene.
2. The method of claim 1 wherein said polynucleotide is introduced by transfection of a suspension of cells *in vitro*.
3. The method of claim 1 wherein said mismatch repair gene is *PMS2*.
4. The method of claim 1 wherein said mismatch repair gene is human *PMS2*.
5. The method of claim 1 wherein said mismatch repair gene is *MLH1*.
6. The method of claim 1 wherein said mismatch repair gene is *PMS1*.
7. The method of claim 1 wherein said mismatch repair gene is *MSH2*.
8. The method of claim 1 wherein said mismatch repair gene is *MSH2*.
9. The method of claim 4 wherein said allele comprises a truncation mutation.
10. The method of claim 4 wherein said allele comprises a truncation mutation at codon 134.
11. The method of claim 10 wherein said truncation mutation is a thymidine at nucleotide 424 of wild-type *PMS2*.
12. The method of claim 1 wherein said polynucleotide is introduced into a fertilized egg of an animal.
13. The method of claim 12 wherein the fertilized egg is subsequently implanted into a pseudo-pregnant female whereby the fertilized egg develops into a mature transgenic animal.
14. The method of claim 12 wherein said mismatch repair gene is *PMS2*.
15. The method of claim 12 wherein said mismatch repair gene is human *PMS2*.
16. The method of claim 12 wherein said mismatch repair gene is human *MLH1*.
17. The method of claim 12 wherein said mismatch repair gene is human *PMS1*.
18. The method of claim 11 wherein said mismatch repair gene is a human *mutL* homolog.
19. The method of claim 15 wherein said allele comprises a truncation mutation.
20. The method of claim 15 wherein said allele comprises a truncation mutation at codon 134.

21. The method of claim 19 wherein said truncation mutation is a thymidine at nucleotide 424 of wild-type *PMS2*.

22. The method of claim 1 wherein said capability is due to the co-introduction of an immunoglobulin gene into said cell.

23. A homogeneous culture of hypermutable, mammalian cells wherein said cells comprise a dominant negative allele of a mismatch repair gene.

24. The culture of hypermutable, mammalian cells of claim 23 wherein the mismatch repair gene is *PMS2*.

25. The culture of hypermutable, mammalian cells of claim 24 wherein the mismatch repair gene is human *PMS2*.

26. The culture of hypermutable, mammalian cells of claim 23 wherein the mismatch repair gene is *MLH1*.

27. The culture of hypermutable, mammalian cells of claim 23 wherein the mismatch repair gene is *PMS1*.

28. The culture of hypermutable, mammalian cells of claim 23 wherein the mismatch repair gene is a human *mutL* homolog.

29. The culture of hypermutable, mammalian cells of claim 23 wherein the cells express a protein consisting of the first 133 amino acids of hPMS2.

30. A method for generating a mutation in a gene affecting antibody production in an antibody-producing cell comprising:

growing a said cell comprising said gene and a dominant negative allele of a mismatch repair gene; and

testing the cell to determine whether said gene of interest harbors a mutation.

31. The method of claim 30 wherein the step of testing comprises analyzing a nucleotide sequence of said gene.

32. The method of claim 30 wherein the step of testing comprises analyzing mRNA transcribed from said gene.

33. The method of claim 30 wherein the step of testing comprises analyzing a protein encoded by the gene of interest.

34. The method of claim 30 wherein the step of testing comprises analyzing the phenotype of said gene.

35. The method of claim 30 wherein the step of testing comprises analyzing the binding activity of an antibody.

36. A method wherein a mammalian cell is made MMR defective by the process of introducing a polynucleotide comprising an antisense oligonucleotide targeted against an allele of a mismatch repair gene into a mammalian cell, whereby the cell becomes hypermutable.

37. The method of claim 36 wherein the step of testing comprises analyzing a nucleotide sequence of said gene.

38. The method of claim 36 wherein the step of testing comprises analyzing mRNA transcribed from said gene.

39. The method of claim 36 wherein the step of testing comprises analyzing a protein encoded by said gene.

40. The method of claim 36 wherein the step of testing comprises analyzing the phenotype of said gene.

41. The method of claim 36 wherein the step of testing comprises analyzing the binding activity of an antibody.

42. A method for generating a mutation in a gene affecting antibody production in an antibody-producing cell comprising:

growing said cell comprising said gene and a polynucleotide encoding a dominant negative allele of a mismatch repair gene; and

testing said cell to determine whether said cell harbors at least one mutation in said gene yielding to a new biochemical feature to the product of said gene, wherein said new biochemical feature is selected from the group consisting of over-expression of said product, enhanced secretion of said product, enhanced affinity of said product for antigen, and combinations thereof.

43. The method of claim 42 wherein the step of testing comprises analyzing the steady state expression of the immunoglobulin gene of said cell.

44. The method of claim 42 wherein the step of testing comprises analyzing steady state mRNA transcribed from the immunoglobulin gene of said cell.

45. The method of claim 42 wherein the step of testing comprises analyzing the amount of secreted protein encoded by the immunoglobulin gene of said cell.

46. The method of claim 36 wherein the cell is made by the process of introducing a polynucleotide comprising a dominant negative allele of a mismatch repair gene into a cell in the presence of DNA mutagens.

47. The method of claim 46 wherein the step of testing comprises analyzing a nucleotide sequence of an immunoglobulin gene of said cell.

48. The method of claim 46 wherein the step of testing comprises analyzing mRNA transcribed from the immunoglobulin gene of said cell.

49. The method of claim 46 wherein the step of testing comprises analyzing the immunoglobulin protein encoded by said gene.

50. The method of claim 46 wherein the step of testing comprises analyzing the biochemical activity of the protein encoded by said gene.

51. A hypermutable transgenic mammalian cell made by the method of claim 42.

52. The transgenic mammalian cell of claim 51 wherein said cell is from primate.

53. The transgenic mammalian cell of claim 51 wherein said cell is from rodent.

54. The transgenic mammalian cell of claim 51 wherein said cell is from human.

55. The transgenic mammalian cell of claim 51 wherein said cell is eukaryotic.

56. The transgenic mammalian cell of claim 51 wherein said cell is prokaryotic

57. A method of reversibly altering the hypermutability of an antibody producing cell comprising introducing an inducible vector into a cell, wherein said inducible vector comprises a dominant negative allele of a mismatch repair gene operably linked to an inducible promoter, and inducing said cell to express said dominant negative mismatch repair gene.

58. The method of claim 57 wherein said mismatch repair gene is *PMS2*.

59. The method of claim 58 wherein said mismatch repair gene is human *PMS2*.

60. The method of claim 57 wherein said mismatch repair gene is *MLH1*.

61. The method of claim 57 wherein said mismatch repair gene is *PMS1*.

62. The method of claim 57 wherein said mismatch repair gene is a human *mutL* homolog.

63. The method of claim 57 wherein said cell expresses a protein consisting of the first 133 amino acids of hPMS2.

64. The method of claim 57 further comprising analyzing the immunoglobulin protein expressed by said antibody producing cell.

65. The method of claim 64 further comprising ceasing induction of said cell, thereby restoring genetic stability of said cell.

66. A method of producing genetically altered antibodies comprising

transfecting a polynucleotide encoding an immunoglobulin protein into a cell, wherein said cell comprises a dominant negative mismatch repair gene;

growing said cell, thereby producing a hypermutated polynucleotide encoding a hypermutated immunoglobulin protein;

screening for a desirable property of said hypermutated immunoglobulin protein;

isolating said hypermutated polynucleotide; and

transfecting said hypermutated polynucleotide into a genetically stable cell, thereby producing a hypermutated antibody-producing, genetically stable cell.

67. The method of claim 66 wherein said mismatch repair gene is *PMS2.*

68. The method of claim 66 wherein said mismatch repair gene is human *PMS2.*

69. The method of claim 66 wherein said mismatch repair gene is *MLH1.*

70. The method of claim 66 wherein said mismatch repair gene is *PMS1.*

71. The method of claim 66 wherein said mismatch repair gene is a human *mutL* homolog.

72. The method of claim 66 wherein said cell expresses a protein consisting of the first 133 amino acids of hPMS2.